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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a **PROVISIONAL APPLICATION FOR PATENT** under 37 CFR 1.53(c)

Attorney Docket No: 01819P0080US

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☒ Additional inventors are being named on the separately numbered sheets attached hereto.

TITLE OF THE INVENTION (280 characters maximum)

Real-Time Simultaneous Analysis and Short-Term Prediction of Heart and Pulse Rate Variability

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ENCLOSED APPLICATION PARTS *(check all that apply)*

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METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT *(check one)*

☐ Applicant claims small entity status (See 37 CFR 1.27.)
☒ A check in the amount of $160.00 is enclosed to cover the filing fee.
☒ The Commissioner is hereby authorized to charge the filing fee, deficiencies in the filing fee, or credit any overpayment to Deposit Account No. 23-0785. A duplicate copy of this sheet is enclosed.

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☒ No.
☐ Yes, the name of the U.S. Government agency and the Government contract number are: _____

Respectfully submitted,

Signature Jeffrey L. Clark

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Date March 26, 2003

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT
Send To: Box Provisional Application, Commissioner for Patents, Washington, D.C. 20231

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PROVISIONAL APPLICATION COVER SHEET
Additional Page

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CERTIFICATE OF MAILING BY EXPRESS MAIL

I hereby certify that this Utility Patent Application Transmittal, enclosed application, and any other documents referred to as enclosed herein, are being deposited in an envelope with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated below and addressed to Box PROVISIONAL APPLICATION, Commissioner for Patents, Washington, D.C. 20231.

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REAL-TIME SIMULTANEOUS ANALYSIS AND SHORT-TERM PREDICTION OF HEART AND PULSE RATE VARIABILITY

FIELD OF THE INVENTION

The present invention relates to the provision of non-stationary and non-linear heart rate variability data, and more particularly to immediate processing, analysis and display of heart rate variability data and its surrogates using non-invasive analysis techniques.

GOVERNMENT SUPPORT

The present invention was made with U.S. Government support from the National Institutes of Health, National Heart, Lung, and Blood Institute, under Grant No. HL 67735, and the National Institute of Neurological Diseases and Stroke, under Grant No. NS 37981. The U.S. Government has certain rights in this invention.

BACKGROUND

Measurements of heart rate and its variability are well known in the art for their usefulness in assessing the conditions of the circulatory system in both health and in disease. They are useful for monitoring many chronic diseases, such as diabetes and heart failure, as well as for monitoring cardiac status during exercise. Particularly useful is Heart Rate Variability (HRV) analysis, which is a non-invasive, clinical tool for assessing the autonomic regulation of cardiac activity. It is also used as a marker of psychophysiological function for biofeedback therapy. Reduced HRV has been associated with such problems as higher long-term risk of post-infarction mortality.

HRV analysis is commonly performed by measuring the beat-to-beat interval between successive heartbeats as collected on an electrocardiogram (ECG). A particularly useful parameter is the period between succeeding "R" waves (the R-R interval), where "R" is the conventional designation given the waveform peak of a normal heartbeat 10 as illustrated in Fig. 1. Most analyses of short-term electrocardiograms using conventional frequency domain HRV techniques (*e.g.*, power spectral density) assume "stationarity" of the underlying R-R interval time series. However, most physiological signals, including heart rate (HR) and pulse rate (PR), are non-stationary by nature. This non-stationarity is a result of complex dynamic interactions among multiple bioregulatory control mechanisms responsible for maintaining homeostasis in the presence of constantly varying physiological and environmental inputs. Additionally, conventional spectral analysis methods are limited by their inability to assess transient changes in HR and PR associated with temporary physical or mental stresses or cardiac pathologies.

Joint time-frequency (t-f) signal processing techniques may be advantageously used over conventional tools for HRV analysis given their ability to analyze time-varying spectral properties of non-stationary signals such as HRV. Such t-f techniques are ideally suited for time-localized spectral characteristics of transient cardiac events that occur as a result of temporal changes in the sympathovagal balance. However, the common use of the Gabor spectrogram, where the short-time Fourier transform is calculated for a window chosen to be appropriate for the data to be collected, may make it difficult to achieve an appropriate compromise between frequency resolution and time resolution.

Techniques such as chaotic analysis have the ability to assess nonlinear, spatio-temporal behavior of such deterministic systems as cardiac activity. Additionally, chaotic analysis has the potential for predictive value in the screening

of patients susceptible to lethal arrhythmias. A numerical "chaotic index" derived from the non-linear analysis of an electrocardiogram or a pulse-rate signal can be used to quantify the degree of non-linear deterministic behavior of cardiac activity. Techniques developed out of chaos theory, such as embedding methods and estimation of Lyapunov exponents, help to unravel the original signal underlying an observed single-variable time series and determine how far into the future it can be predicted. Chaotic systems comprise a class of signals that lies between predictable periodic or quasi-periodic signals and totally irregular stochastic signals which are completely unpredictable. The Lyapunov exponent measures the sensitivity of the system to initial conditions and thus provides a measure to help predict the short-term behavior of the system.

Such HRV analysis has heretofore typically been performed by hooking a patient up to equipment for monitoring heart activity and storing the data from the monitored heart activity. After monitoring heart activity has been accomplished for a sufficient period of time so that a selected amount of data has been accumulated (*e.g.*, from several minutes to several hours), the data are transferred to a computer in which they are analyzed to provide the physician with such information as the Chaotic Index (the largest Lyapunov exponent [measure of degree of chaos] calculated using the data represented by the heart rate [or pulse rate] sequence), BPM (beats per minute [Heart Rate or Pulse Rate]), SDNN (standard deviation of R-R intervals [or inter-pulse intervals] derived from the electrocardiogram [or pulse plethysmograph] data after putative abnormal R-R intervals [or inter-pulse intervals] are removed), and RMSSD (root-mean-square of the difference between successive R-R intervals [or inter-pulse intervals] derived from the electrocardiogram [or pulse plethysmograph] data). The generated information is then reviewed by a physician, typically long after the heart activity which was used to generate the

information has taken place, and the physician uses the generated information at that later time to determine a status or treatment procedure for the patient. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Heart Rate Variability: Standards of Measurement, Physiological Interpretation, and Clinical Use.* Circulation, 93(5), pp1043-1065, 1996; Goldberger AL, Amaral LAN, Glass L, Hausdorff JM, Ivanov PCh, Mark RG, Mietus JE, Moody GB, Peng CK, Stanley HE. PhysioBank, PhysioToolkit, and Physionet: *Components of a New Research Resource for Complex Physiologic Signals.* Circulation 101(23): e215-e220 and U.S. Patent Nos. 5,265,617, 5,437,285, 5,682,901, 5,842,997, 5,957,855, 6,115,629, 6,416,471, 6,480,733, and 6,485,416 variously teach HR monitoring and analysis, and their full disclosures are hereby incorporated by reference.

While such analysis has had value in the treatment of a patient, the delay in the analyzed data provided to the physician has clear disadvantages. For example, the physician's receipt of analyzed data may be so delayed as to cause the initiation of an action, such as a treatment, to be disadvantageously delayed, or in the worst case the information may be generated too late to be of help in treating the patient. As another example, the review of such information by a physician hours after the data were collected may make it difficult to correlate the data with other conditions of the patient for which data were not being simultaneously recorded. A physician will observe many things when with a patient, but hours later may be unable to temporally correlate many of those observations with the corresponding HRV data. Still further, it should be appreciated that prior art HRV information which has been generated based on a selected set of data has in many ways been able to present only a static picture of a dynamic situation.

The present invention is directed toward overcoming one or more of the problems set forth above.

SUMMARY OF THE INVENTION

Since HRV is an important measure of the condition of the heart, which could change rapidly, it is particularly important to be able to perform real-time HRV analysis while the heart rate is being measured. No current system is able to perform such detailed HRV analysis and display the results in real time. The present invention relates to a system and method that can simultaneously acquire electrocardiogram or pulse rate data, dynamically perform time-frequency (t-f) and chaotic analysis in real-time, visually display the results in a convenient graphical format and store the results in a computer file format. The system and method can provide a real-time automated system that combines the non-stationary analysis capability for evaluating cardiac signal histories with a predictive capability of non-linear analysis to better monitor and categorize autonomic regulation of cardiac function. This system allows for continuous, real-time monitoring of cardiac function and enables short-term prediction of cardiac activity under autonomic control.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 illustrates a waveform of a conventional heart beat;

Figure 2 is an example computer and data acquisition device which may be used in accordance with the present invention;

Figure 3 is a monitor showing an example screenshot from the system performing HRV analysis on pre-acquired representative data for a normal electrocardiogram;

Figure 4 is a flowchart illustrating the overall process of data acquisition, analysis and display of the real-time HRV or pulse rate variability (PRV) analysis system according to the present invention, where Figs. 5-9 are detailed flowcharts of portions of the Fig. 4 process:

Figure 5 is a flowchart illustrating the initiation of analysis and data acquisition;

Figure 6 is a flowchart illustrating details of the event detection step;

Figure 7 is a flowchart illustrating details of heart rate resampling and RR sequence generation;

Figure 8 is a flowchart illustrating details of determining time-frequency distribution; and

Figure 9 is a flowchart illustrating details of non-linear data analysis;

Figures 10A-10C are sequential pages of an algorithm in Visual C++ programming language which may be used to detect the peaks in the R wave and to compute the R-R interval;

Figure 11 is an example screenshot from the system performing HRV analysis on pre-acquired representative data for a Chronic Heart Failure (CHF) electrocardiogram; and

Figure 12 is an example screenshot from the system performing HRV analysis on pre-acquired data representative of an epileptic seizure episode electrocardiogram.

The accompanying drawings, which are incorporated in and form a part of this specification, illustrate embodiments of the invention and, together with descriptions, serve to explain the principles of the invention. They are not intended to limit the scope of the invention to the embodiments described. It is appreciated

that various changes and modifications can be made without departing from the spirit and scope of the invention as defined in the appended claims.

DETAILED DESCRIPTION OF THE INVENTION

Fig. 2 illustrates a device which may be used in accordance with the present invention. As illustrated, the device comprises a suitable processing unit, such as a personal computer 12 with a suitable CPU, a user input device 14 (such as the illustrated keyboard, and/or other suitable devices such as a mouse, touch-screen, or keypad-controlled graphic user interface), and suitable display device such as a CRT monitor 16, and a suitable data acquisition device 18 which may be attached to a patient to obtain ECG data of a patient's heart.

In order to facilitate processing of the various elements of HRV analysis which may be performed in real-time in accordance with the present invention, a suitable processor with architecture for performing specific functions may be advantageously used with the computer 12. For example, Intel Corporation's IPP ("Integrated Performance Primitives") for its Pentium® processors and Itanium® architecture permit a variety of operations which are performed in connection with the present invention to be quickly performed, and may therefore be advantageously used in a computer 12 used with the present invention. For example, where Visual C++ based software code is used to perform the operations providing the desired HRV analysis, the following operations may be performed using IPP function calls: memory allocation and deallocation, array initialization, freeing of memory, calculating means, absolute values and exponentials for array elements in multidimensional arrays, Fast Fourier Transforms and Inverse Fast Fourier Transforms. Use of such IPP function calls permit such functions to be performed with significantly fewer lines of software code than would be required to perform

such functions with normal processing, and therefore can significantly speed up the processing functions to allow analysis to stay in real-time as the processes are continuously updated as discussed in further detail below.

Suitable ECG data acquisition devices 18 acquire heart beat data such as is known in the art, and are available from, for example, QRS Diagnostic, LLC of Plymouth, Minnesota, U.S.A., which have devices which may be connected directly to a serial port on a PC processing unit without requiring special hardware to communicate through the serial port. However, it should be understood that many different data acquisition devices may also be advantageously used within the scope of the invention including, for example, devices which may be directly connected to different computer ports, such as PCMCIA ports conventionally found in laptop computers. In addition, a battery-powered device, such as a cell phone, PDA, or tablet PC may be used in combination with an electrocardiogram or finger pulse sensor, for acquisition, transmission and remote monitoring of heart rate variability or pulse rate variability parameters. Further, it should be recognized that multiple devices may be used with a single computer (whether other computer components or other ECG data acquisition devices), with the connection to the ECG data acquisition device of interest (connected to the patient of interest) being selectable by the user. As another example, it should be appreciated that the present invention may utilize a battery-powered, Class II biofeedback prescription device, such as a PDA or a battery powered computer, in combination with a finger pulse sensor or ECG acquisition system.

Further, as detailed herein, the data acquisition device 18 may be used in connection with the present invention to provide data for real-time analysis simultaneously with its collection, or may acquire data which is suitably stored (*e.g.*, on the hard drive of a personal computer 12) in a form which preserves moment-to-

moment correlative relationships so that they can be retrieved electronically for later playback or as hard copy for later review and/or documentation.

Fig. 3 is an example of a video display on a monitor 16 of the HRV analysis of a normal ECG in accordance with the present invention, where the data being analyzed have been pre-acquired:

Graphic display element 20 illustrates in wave form the unprocessed electrocardiogram or pulse data of the pre-acquired data file;

Graphic display element 22 is the heart rate or pulse rate derived from the electrocardiogram or pulse data;

Graphic display element 24 is an intensity-mapped time-frequency distribution color contour plot, with its time axis (the horizontal axis) shared with the time axis of display element 22;

Graphic display element 26 is the electrocardiogram or pulse attractor ("ECG attractor") derived from the electrocardiogram or pulse data;

Graphic display element 28 is the play button for pre-acquired data processing (if operated while the data are being acquired from a patient, the element 28 functions as a start button);

Graphic display element 30 is the stop button both for pre-acquired data processing and for the mode of operation in which the data are processed real-time as it is acquired from a patient; and

Graphic display element 32 is the dialog box for reporting system status.

In the example shown, the heart rate is 117 beats per minute, the SDNN is 88 ms, the RMSSD is 22 ms, the SI/PI ratio (discussed further below) is 1.3, and the Chaotic Index is 0.41. Moreover, as detailed hereafter, this information is dynamic in that it is analyzed and modified over real time. That is, even when used with a file of pre-acquired data, the analysis and display of the data and analysis occurs

dynamically over time corresponding to the passage of time which occurred when the data were acquired. It should also be appreciated that when used as the data are being acquired, as discussed herein, the analysis and display of the data and analysis, occurs dynamically as the dynamic event (*i.e.*, patient heart beat) occurs.

Fig. 4 is a flow chart illustrating the dynamic, real time HRV analysis which may be performed in accordance with the present invention. Further details of this operation illustrated in overview in Fig. 4 are set forth hereinafter, including in Figs. 5-9 and in the associated written specification.

Specifically, at box 40 the user inputs data parameters such as detailed further below. Such data parameters may be used to control the analysis mode and output generation, including whether analysis is to be performed using an external data source (at 42) or a file of pre-acquired electrocardiogram or pulse waveform data (at 44). Such parameters can further include, for example, sampling frequency for real time data acquisition, or selection of the file which has the pre-acquired data of interest. The data to be used (such as unprocessed ECG data or pulse plethysmograph data) and the parameters to use in connection with its analysis are then received at box 46. This process is set forth in greater detail in Fig. 5 below.

The unprocessed data at box 46 are sent (as indicated by arrow 48) to a suitable display such as a CRT monitor as illustrated in Fig. 3 for graphic display of the waveform in real time (such as illustrated as graphic display element 20 in Fig. 3).

The data at box 46 are additionally analyzed using the user input parameters in accordance with the present invention. That is, the data may be used at box 52 to generate an ECG attractor (as set forth in greater detail in Fig. 9 below) and then displayed as graphical display element 26 (Fig. 3). This graphical

"attractor" can be derived, in real-time, from the raw electrocardiogram or pulse rate signal to visually represent the temporal evolution of cardiac dynamics in multidimensional space. Chaotic systems exhibit complex trajectories that do not converge to a fixed point or cross each other as the trajectories evolve over time, while periodic trajectories follow a cyclical path. The data at box 46 may also be analyzed to detect a QRS event at box 54 from which a RR time sequence or inter-pulse sequence may be generated at box 56 (as set forth in greater detail in Fig. 6 below).

The RR time sequence (or inter-pulse sequence) may be used for further HRV analysis, including determining a Chaotic Index at box 60 (as described in greater detail in Fig. 9 below), and determining time domain parameters at box 62 such as heart rate or pulse rate, RMSSD and SDNN (as described in greater detail in Fig. 7). All of these time domain parameters may be displayed at box 50 such as illustrated in Fig. 3.

The RR time sequence (or inter-pulse sequence) may further be used at box 64 to generate a heart rate (HR) or pulse rate (PR) time sequence or series (as described in greater detail in Fig. 7 below), which may be sent (as indicated by arrow 66) for display as graphical display element 22 (see Fig. 3). Further, the HR time sequence or series may be used at box 70 for time-frequency (t-f) distribution analysis, including generating and displaying an intensity based color-mapped contour plot (as indicated by arrow 72) and generating (at box 74) and displaying (at box 50) SI, PI and SI/PI indexes (as described in greater detail in Fig. 8 below).

Fig. 5 illustrates the initiation of the analysis mode and data acquisition. Specifically, the user first inputs the analysis mode at box 120, indicating whether operation is to use data being acquired at the time from a patient, or operation is to use pre-acquired data.

If pre-acquired data is to be used, decision box 122 proceeds to list the available files of pre-acquired data at box 124, and the user selects the desired file at box 126. If the user wishes to perform the analysis using a sampling frequency which is other than the default sampling frequency indicated at box 128 (*e.g.*, 500 Hz which detects the electrical signal of the heart 500 times per second), he may do so at box 130, in which case the sampling frequency may be changed to a different selected value at box 132. This may be required, for example, when the pre-acquired data of the selected file was acquired using a different sampling frequency than the default sampling frequency. Whatever sampling frequency is selected, the data from the selected file of pre-acquired data is then sequentially read at box 134 in time order.

Alternatively, if analysis is to occur as the data is being acquired, a determination may first be made by the user at box 140 as to whether or not the computer port receiving the data from the ECG data acquisition device is connected to the default port (*e.g.*, a computer serial port such as previously described). In that case, if the user does not indicate at box 140 that a port different than the default port (*e.g.*, COM Port 4) is to be used, then processing continues at box 142 with data acquisition occurring through the default port. If the user selects a different port, then the selected different port is set at box 144 to be recognized as receiving the data. Once the proper port for receiving data is set, the computer then begins to acquire data at box 146 from the ECG data acquisition device.

As that data are acquired, whether from the computer file of pre-acquired data at a selected sampling frequency (at box 134) or from the ECG data acquisition device (at box 146), the data may at box 148 be displayed on the monitor 16 to show the ECG waveform, which display may be updated periodically (*e.g.*, every 0.1 seconds).

As sequential data are acquired according to the above, processing of the data then proceeds, including event detection 150 (Fig. 5) and non-linear analysis 152 (Fig. 9, discussed further below).

Event detection as illustrated in Fig. 6 involves determination of a QRS event in a sequential set of data points in a time series of ECG data, which may be characterized as *data(t)*. As is recognized by those skilled in the art, the ECG waveform of a standard heartbeat is illustrated in Fig. 1, with the standard peaks in that waveform having the conventional designations P, Q, R, S and T. Detection of a QRS event is the detection of an ECG waveform in the form of points Q, R and S. Engelse, W.A.H., and Zeelenberg, C.: *A Single Scan Algorithm for QRS-Detection and Feature Extraction*. Computers in Cardiology 6, 37-42, 1979 teaches QRS event detection, and the full disclosure thereof is hereby incorporated by reference herein.

Initial filtering of the data first occurs. For example, a differentiator with a 62.5 Hz notch filter is applied at box 220, where:

$$Y0(t) = data(t) - data(t-4)$$

Such a differentiator filters out power line noise conventionally found at around 62.5 Hz, as is explained in Friesen, G.M., Jannett, T.C., Jadallah, M.A., Yates, S.L., Quint, S.R., and Nagle, H.T.: *A Comparison of the Noise Sensitivity of Nine QRS Detection Algorithms*. IEEE Transactions on Biomedical Engineering, BME-37 (1), pp85-98, 1990, the complete disclosure of which is hereby incorporated by reference. In addition to filtering out power line noise, a low pass filter may also be applied at box 222 to filter out high frequency noise, where:

$$Y1(t) = Y0(t) + 4*Y0(t-1) + 6*Y0(t-2) + 4*Y0(t-3) + Y0(t-4)$$

Such a suitable filter is also explained, for example, in Friesen *et al.*

After the data have been suitably filtered, it is determined at box 224 whether Y1(t) (which is the slope of the ECG waveform) has exceeded a threshold. If it has not, then no R peak of a QRS event has occurred, in which case it is determined at box 226 whether or not all of the current ECG data have been analyzed. If there are more data for analysis, processing begins again at box 224 to determine whether Y1(t+1) has exceeded the threshold.

As the data points are sequentially processed according to the above, if the slope of the data points are found to exceed the threshold at box 224, it is then determined at box 230 whether or not crossing of the threshold occurred within the search region. If it did not, then the high slope is interpreted at box 232 as being a baseline shift, such as can occur from, for example, breathing, movement of the patient, or a change in the contact of the electrodes with the patient's skin. If it is determined at box 240 that the threshold crossings of the data points within the search region meet the established QRS event criteria (*i.e.*, essentially indicates that the peak in the waveform is high enough to be an R peak), then the event is classified at box 244 as a QRS event. If it is determined at box 240 that the threshold crossings of data points within the search region do not meet the established QRS event criteria, then the event is classified as noise at box 246.

Once all of the current ECG data have been analyzed as determined at box 226 so that a QRS event has been detected, heart rate resampling and RR sequence generation (of the RR time series) proceeds at box 250. The RR time series may then be used in non-linear analysis at box 152 as discussed further below in connection with Fig. 9.

Heart rate resampling and RR sequence generation is illustrated in Fig. 7. At box 320, the location of R peaks as data points are identified (based on where QRS events were identified during event detection described above in

connection with Fig. 6). With the R peak data points identified, a sampling rate is chosen at box 322 for the heart rate signal (*e.g.*, sampling frequency/100), such as is shown in Berger, R.D., Akselrod, S., Gordon, D., and Cohen, R.J., *An Efficient Algorithm for Spectral Analysis of Heart Rate Variability.* IEEE Transactions on Biomedical Engineering, BME-33 (9), pp900-904, 1986, the full disclosure of which is hereby incorporated by reference. The number of RR intervals (*i.e.*, the interval from one R peak to the next R peak of a waveform) contained within a local window (*e.g.*, 100 data points) of the heart rate signal is then calculated at box 326, and the instantaneous heart rate is calculated at box 328 as:

HR = f * n/2, where f = sampling frequency, and n = number of RR intervals.

The local window of data points is then slid forward (*e.g.*, 100 points) at box 330 and, if it is determined at box 332 that the end of the current ECG time series has not been reached, the number of RR intervals and the instantaneous heart rate is calculated for the new window of data points at boxes 328 and 330 as described. When it is determined at box 332 that the end of the time series has been reached, the heart rate time series may be displayed at box 336 and processing of a time-frequency distribution may proceed at box 340.

In addition to the heart rate resampling in boxes 322-332, time domain parameters may be simultaneously determined based on the location of the R peaks identified at box 320. The calculation of time domain parameters is usually based on the NN interval, as opposed to the RR interval. Therefore, potential ectopic beats should be removed from the calculation. In this calculation therefore, ectopic beats may be identified and removed at box 350, for example by determining that if the RR interval duration is more than 15% different than the previous RR interval, such a beat would be taken to be ectopic and then removed. That is, if abs[RR(i)/RR(i-1) - 1] > 0.15, then the beat at time "i" is taken as being ectopic and

is removed. Checking for ectopic beats, and removing those identified ectopic beats at box 350 is continued until it is determined at box 352 that data with ectopic beats removed have been collected for a five minute period, at which point SDNN and RMSSD may be calculated at box 354 as follows:

RMSSD = sqrt(sum(sqr(rr(n)-rr(n-1)), N)/N)

SDNN = stdev(n, N)

After SDNN and RMSSD have been calculated, they are displayed at box 356.

Determination of time-frequency distribution is shown in Fig. 8. Joint time-frequency distributions may be used to depict the time-varying behavior of signals of which the frequency content is of interest. Use of one of the Wigner-Ville family of time-frequency distributions make it possible to achieve an appropriate compromise between frequency resolution and time resolution. As illustrated in Fig. 8, a uniformly sampled HR time series is obtained at box 420 such as previously described in connection with boxes 320-340 (Fig. 7). The HR time series is then converted at box 422 to an RR time series, where:

RR(t) = 60,000/HR(t)

The time-frequency distribution for the RR time series is then calculated at box 426 using the kernel function which is empirically determined to be optimal, such as described in Pola, S., Macerata, A., Emdin, M., and Marchesi, C., *Estmation of the Power Spectral Density in Nonstationary CardioVascular Time Series: Assessing the Role of the Time-Frequency Representations (TFR)*. IEEE Transactions on Biomedical Engineering, Vol. 43, No. 1, pp 46-49, the complete disclosure of which is hereby incorporated by reference.

Joint t-f distribution analysis mathematically decomposes the RR time series into time-varying components of the frequency spectra. These frequency-domain calculations result in three main HRV spectral components: very low fre-

quency (VLF), low frequency (LF), and high frequency (HF). The LF component (0.04 to 0.15 Hz) has been associated mainly with sympathetic activity while the HF component (0.15 to 0.40 Hz) has been correlated with parasympathetic activity. There is a constant interplay between these autonomic stimuli to influence HR. The resulting sympatho-vagal balance can be quantified by using the ratio of LF to HF spectral power. In this context, analysis using frequency methods has been found to be a better predictor of physiologic changes than time-domain methods.

An SI index, PI index and SI/PI ratio may be calculated (and displayed) at boxes 430, 432 and 436. The SI index is the spectral power in the 0.04 Hz to 0.15 Hz low frequency range of the t-f distribution integrated over the entire time duration of the t-f distribution displayed on the computer screen, the PI index is the spectral power in the 0.15 Hz to 0.40 Hz high frequency range of the t-f distribution integrated over the entire time duration of the t-f distribution displayed on the computer screen, and the SI/PI ratio is the ratio of SI spectral power to PI spectral power. The SI/PI ratio is a quantification of the above mentioned sympathovagal balance. The SI index, PI index and SI/PI ratio correspond to the moment by moment predominantly sympathetic tone, parasympathetic tone, and sympatho-vagal balance, respectively.

The time-frequency distribution for the RR time series calculated at box 426 may also be color mapped according to spectral power intensities at box 450, and the intensity-mapped color display representing that distribution may be displayed at box 452. More specifically, the color mapping consists of converting the time-frequency (t-f) distribution values to color-coded intensity maps which have been found to visually illustrate certain data conditions which a physician may find useful. This color mapping may be accomplished by determining the maximum value (global max) of the t-f distribution for the entire time and frequency range for

the RR interval sequence being analyzed. The frequency range may be fixed to limits corresponding to the ranges used for computing SI and PI, namely:

Hf_max = 0.4 Hz

Hf_min = 0.15 Hz

Lf_max = 0.15 Hz

Lf_min = 0.04 Hz

hfreq = 0.5 Hz

For each time slice to be displayed, the local minimum and maximum values of the t-f distribution are evaluated over the frequency range from Lf_min to hfreq (*e.g.*, from 0.04 Hz to 0.5 Hz), with the local minimum value being defined as the single lowest power value in that frequency range and the local maximum value being the data point with the highest power value that is greater than the power of its two preceding and two succeeding neighbors in the range. A weighted average time-slice maximum (M_{WA}) is then calculated:

$$M_{WA} = 0.9 \text{ local max} + 0.1 \text{ Global max}$$

For each time slice, the color value for each point in the t-f distribution is calculated as follows:

$$\text{Color value} = (\text{Power value} - \text{local min}) / (M_{WA} - \text{local min})$$

The color value is then mapped using a table of, for example, 256 rainbow colors ranging from black to white. The following is an example of a table which may be suitably used to map the color value in RGB (Red, Green, Blue) format:

Intensity	R	G	B		Intensity	R	G	B		Intensity	R	G	B
0	0	0	0		1	45	0	36		2	56	0	46
3	60	0	49		4	67	0	54		5	70	0	59
6	71	0	61		7	75	0	68		8	74	0	73
9	74	0	77		10	73	0	81		11	71	0	87
12	69	1	90		13	68	2	94		14	66	3	97

Intensity	R	G	B	Intensity	R	G	B	Intensity	R	G	B
15	63	6	102	16	67	1	106	17	58	10	109
18	56	12	113	19	53	15	116	20	48	18	119
21	47	20	121	22	44	23	124	23	41	27	128
24	40	28	129	25	37	32	132	26	34	36	134
27	29	43	137	28	25	52	138	29	24	57	139
30	24	62	141	31	24	64	142	32	23	65	142
33	23	69	143	34	23	71	142	35	23	71	142
36	23	73	142	37	23	75	142	38	23	75	142
39	23	78	142	40	23	80	142	41	23	80	142
42	23	82	141	43	23	85	141	44	23	85	141
45	23	87	140	46	24	87	140	47	24	90	140
48	24	90	140	49	24	93	139	50	24	93	139
51	24	93	139	52	24	93	139	53	24	97	139
54	24	97	139	55	25	101	138	56	25	101	138
57	25	104	137	58	25	104	137	59	25	104	137
60	26	108	137	61	26	108	137	62	27	111	136
63	27	111	136	64	27	111	136	65	27	115	135
66	27	115	135	67	28	118	134	68	28	118	134
69	29	122	133	70	29	122	133	71	29	122	133
72	29	122	133	73	29	125	132	74	29	125	132
75	30	128	131	76	30	128	131	77	31	131	130
78	31	131	130	79	31	131	130	80	32	134	128
81	32	134	128	82	33	137	127	83	33	137	127
84	33	137	127	85	34	140	125	86	34	140	125
87	35	142	123	88	35	142	123	89	36	145	121
90	36	145	121	91	36	145	121	92	37	147	118
93	37	147	118	94	38	150	116	95	38	150	116
96	40	152	113	97	40	152	113	98	41	154	111
99	41	154	111	100	42	156	108	101	42	156	108
102	43	158	106	103	43	158	106	104	43	158	106
105	45	160	104	106	45	160	104	107	46	162	101
108	46	162	101	109	48	164	99	110	48	164	99
111	50	166	97	112	50	166	97	113	51	168	95
114	53	170	93	115	53	170	93	116	53	170	93
117	55	172	91	118	55	172	91	119	57	174	88
120	57	174	88	121	59	175	86	122	62	177	84
123	64	178	82	124	64	178	82	125	67	180	80
126	67	180	80	127	69	181	79	128	72	183	77

Intensity	R	G	B	Intensity	R	G	B	Intensity	R	G	B
129	72	183	77	130	72	183	77	131	75	184	76
132	77	186	74	133	80	187	73	134	83	189	72
135	87	190	72	136	91	191	71	137	95	192	70
138	99	193	70	139	103	194	70	140	107	195	70
141	111	196	70	142	111	196	70	143	115	196	70
144	119	197	70	145	123	197	70	146	130	198	71
147	133	199	71	148	137	199	72	149	140	199	72
150	143	199	73	151	143	199	73	152	147	199	73
153	150	199	74	154	153	199	74	155	156	199	75
156	160	200	76	157	167	200	78	158	170	200	79
159	173	200	79	160	173	200	79	161	177	200	80
162	180	200	81	163	183	199	82	164	186	199	82
165	190	199	83	166	196	199	85	167	199	198	85
168	199	198	85	169	203	198	86	170	206	197	87
171	212	197	89	172	215	196	90	173	218	195	91
174	224	194	94	175	224	194	94	176	230	193	96
177	233	192	98	178	236	190	100	179	238	189	104
180	240	188	106	181	240	188	106	182	242	187	110
183	244	185	114	184	245	184	116	185	247	183	120
186	248	182	123	187	248	182	123	188	250	181	125
189	251	180	128	190	252	180	130	191	253	180	133
192	253	180	133	193	254	180	134	194	254	179	138
195	255	179	142	196	255	179	145	197	255	179	145
198	255	179	152	199	255	180	161	200	255	180	164
201	255	180	167	202	255	180	167	203	255	181	169
204	255	181	170	205	255	182	173	206	255	183	176
207	255	183	176	208	255	184	179	209	255	185	179
210	255	185	182	211	255	186	182	212	255	185	182
213	255	187	185	214	255	188	185	215	255	189	188
216	255	189	188	217	255	190	188	218	255	191	191
219	255	192	191	220	255	194	194	221	255	194	194
222	255	197	197	223	255	198	198	224	255	200	200
225	255	201	201	226	255	201	201	227	255	202	202
228	255	203	203	229	255	205	205	230	255	206	206
231	255	206	206	232	255	208	208	233	255	209	209
234	255	211	211	235	255	215	215	236	255	216	216
237	255	216	216	238	255	218	218	239	255	219	219
240	255	221	221	241	255	223	223	242	255	226	226

Intensity	R	G	B	Intensity	R	G	B	Intensity	R	G	B
243	255	228	228	244	255	230	230	245	255	230	230
246	255	232	233	247	255	235	235	248	255	237	237
249	255	240	240	250	255	243	243	251	255	246	246
252	255	249	249	253	255	251	251	254	255	253	253
Default	255	255	255								

Graphic display element 24 illustrates an intensity-mapped time-frequency distribution color contour plot, with its time axis (the horizontal axis) shared with the time axis of display element 22.

Non-linear analysis may also be performed using the RR time series (from box 250, Fig. 6) and data waveform (from box 148, Fig. 5) as illustrated in Fig. 9.

Specifically, one analysis which may be performed is to use the data point time series for the waveform, whether received from the ECG device or a pre-acquired data file (from box 148, Fig. 5), to generate at box 522 a XY scatter plot conventionally known as an "ECG attractor". As is known to those skilled in the art, the original ECG time series (*i.e.*, data(t)) is used as the Y-coordinate and its time-embedded equivalent time series (*i.e.*, data(t-tau)) is used as the X-coordinate, where tau equals two ECG sample intervals. That is, a delay filter is used to generate the nth dimension of data from the (n-1) dimension. In the illustrated example, a static delay of two sample intervals is used to generate the second dimension, although it should be understood that this can be extended to more dimensions and different delays. The XY scatter plot of the ECG attractor is displayed at box 524.

In another similar non-linear analysis (using the RR time series from box 250, Fig. 6, whereas the graphical representation of the ECG attractor of box 522 uses the raw ECG waveform from box 148, Fig. 5), a two-dimensional XY time series characterized as an RR attractor is generated at box 530 using the RR time

series as the Y-coordinate and its time embedded equivalent time series as the X-coordinate, with a time delay equal to two RR sample intervals. The nearest neighbor and its separation from the initial point is then determined at box 532. If the spatial separation is determined at box 534 to be greater than a selected threshold, then Gram-Schmidt reorthonormalization is performed at box 536 on the vector defined by the two points and then the step of box 532 is repeated until the separation does not exceed the threshold for renormalization (as determined at box 536), at which point the principal axis vector can be obtained at box 538. The principal axis vector may then be used at box 540 to estimate the largest Lyapunov exponent, conventionally known as the Chaotic Index, which is a measure of the degree of chaos. Algorithms for calculating Chaotic Index are known in the art, such as shown in Wolf MM, Varigos GA, Hunt D, Sloman, JG. *Sinus arrhythmia in acute myocardial infarction*. Med. J. Aust., 2 pp 52-53, 1978, the complete disclosure of which is hereby incorporated by reference.

The Chaotic Index may then be displayed at box 542. Determining and periodically monitoring the Lyapunov exponent for a physiological system over an extended length of time could reveal additional trends towards less or more chaotic behavior which may be indicative of a progressive disease requiring pharmaceutical or therapeutic intervention or an adjustment of a treatment regimen.

In accordance with the present invention, the above data analysis may be performed in a dynamic manner by refreshing the analysis in real-time (where real-time is used herein as referring not only to analysis occurring while external data are being received but also to dynamic analysis of pre-acquired data as those data are played back over a time period essentially corresponding to the time period for which the data were previously acquired).

More specifically, as indicated in Fig. 4, the ECG or pulse waveform may be continuously updated to display a waveform at box 50 based on, as an example, a batch of 4,096 data points received at box 46. At a 500 Hz sampling frequency (comprising 500 samples per second), 4,096 data points comprise approximately eight seconds of data. Those same 4,096 data points are also XY plotted at box 52 and displayed at box 50 as the ECG attractor.

Those same 4,096 data points are also processed for event detection (see Fig. 6) at box 54, with a continuous output of detected QRS events used to generate a continuous RR sequence (RR time series) at box 56 (see box 250, Fig. 6). With event detection being accomplished within the time frame of the batch of data points being processed (*e.g.*, approximately eight seconds for 4,096 data points at a 500 Hz sampling frequency), receipt and event detection for the next batch of 4,096 data points may be accomplished in real-time (*i.e.*, in keeping with the time element of the data points).

While the event detection may be accomplished with a batch of data points, each detected RR interval may nevertheless be output to box 56 (generating the RR time series) as it is detected (*i.e.*, before event detection is completed for all 4,096 data points). Therefore, it should be appreciated that at this point in the continuous processing after box 56 in Fig. 4, analysis will occur using RR intervals as "points" rather than raw data points as used in box 54.

Specifically, the Chaotic Index may be determined at box 60 for every 128 RR intervals as determined at box 56. Therefore, once the first 128 RR intervals have been determined, the Chaotic Index will be calculated (see box 540, Fig. 9) and displayed until another group of 128 RR intervals have been determined, at which point a new Chaotic Index will be similarly calculated and the displayed Chaotic Index will change to the newly calculated Chaotic Index.

The time domain parameters (HR or PR, RMSSD, SDNN) determined at box 62 are also calculated using RR intervals as data points. These parameters are first calculated and displayed when five minutes worth of RR interval data have been accumulated, and then may be recalculated and displayed thereafter every time a new RR interval data point is received. Thus, the SDNN parameter is the standard deviation of RR intervals (or inter-pulse intervals) derived from a 5 minute time segment of electrocardiogram (or pulse plethysmograph) data after putative abnormal RR intervals (or inter-pulse intervals) are removed (at box 350 in Fig. 7), and the RMSSD parameter is the root-mean-square of the difference between successive RR intervals (or inter-pulse intervals) from the same 5 minute segment of electrocardiogram (or pulse plethysmograph) data.

Processing beyond box 64 uses HR sequence (HR time series), which is a conversion of the RR time series to a time series having a uniform interval (see box 420, Fig. 8). Those data may then be displayed (per arrow 66) to display 256 uniform interval points accumulated in forty point batches. The data may similarly be used in such 256 point groupings for time-frequency (t-f) distribution analysis, from which the SI, PI and SI/PI indexes may be calculated at box 72 (see boxes 430-436 of Fig. 8) and then displayed and the t-f distribution spectral power intensities color mapped and displayed (boxes 450-452 of Fig. 8). Color mapping and index calculation may be performed using a moving window of 256 HR interval points (from box 64), updated every 64 points. That is, when 256 HR interval points are first received, mapping and index calculation will occur with the results displayed until an additional 64 HR interval points are received, at which point the first 64 HR interval points in the prior batch will be dropped and then mapping and index calculation will again be done using the last 192 HR interval points from the prior batch and the new 64 HR interval points.

It should be recognized that the present invention is not limited to the above details relating to suitable processing of data points, including the particular numbers of points used in individual calculations. However, it should be appreciated that the above described manner of processing the received heart beat data has been found to be suitable in providing the desired real-time analysis, with the attendant advantages to physician knowledge and patient care. It should also be appreciated that instead of patient treatment, the method and system of the present invention could be used for alternative purposes, such as relaxation training.

It should also be appreciated that much of the above may be accomplished using suitable software performing the described processing and display. Visual C++ is one suitable programming language which may be used, as illustrated by Figs. 10A-10C which sets forth a Visual C++ programming language algorithm for detecting the peaks in the R wave and computing the R-R interval (for QRS event detection, as shown in Fig. 6).

Figs. 11-12 illustrate screenshots displaying the data and analysis processed according to the above description for abnormal conditions, with Fig. 11 illustrating an example HRV analysis on pre-acquired representative data for a Chronic Heart Failure (CHF) electrocardiogram and Fig. 12 illustrating an example HRV analysis on pre-acquired data representative of an epileptic seizure episode electrocardiogram. As can be seen in Fig. 11, the HRV analysis for the example Chronic Heart Failure (CHF) electrocardiogram results in a display of a heart rate of 65 beats per minute, an SDNN of 36 ms, an RMSSD of 27 ms, an SI/PI ratio of 0.4, and a Chaotic Index of 0.04. In Fig. 12, by contrast, where the input data involve an epileptic seizure episode, the heart rate is 60 beats per minute, the SDNN is 238 ms, the RMSSD is 30 ms, the SI/PI ratio is 1.4, and the Chaotic Index is 0.60. The differences in the displayed information between the normal condition

of Fig. 3 and the different abnormal conditions of Figs. 11-12 (the various displayed indices, as well as the displayed plots [*e.g.*, electrocardiogram, heart rate, intensity-mapped time-frequency distribution color contour plot, electrocardiogram attractor]) provide an important new tool for the development of a detailed understanding of the dynamic mechanisms underlying the conditions represented, and may provide distinct and valuable data to a treating physician who, when provided in real-time as the patient undergoes the abnormal condition, can be assured of having the most up to date information for evaluation as he evaluates possible treatments.

The system and method of the present invention provide a new tool for real-time automated analysis of heart rate variability and its adjuncts, that combine the non-stationary analysis capability for evaluating cardiac signal histories with the predictive capability of non-linear analysis to better monitor and categorize autonomic regulation of cardiac function.

Still other aspects, objects, and advantages of the present invention can be obtained from a study of the specification and the drawings. It should be understood, however, that the present invention could be used in alternate forms where less than all of the objects and advantages of the present invention and preferred embodiment as described above would be obtained.

CLAIMS

1. A method of monitoring variability of heart activity occurring during a time period, comprising the steps of:

sequentially receiving data points of heart activity data over a period of time corresponding to the time period of the heart activity;

evaluating said data points as sequentially received to determine QRS events;

outputting said QRS events to a processor as they are sequentially determined;

processing said output QRS events as they are output to periodically determine heart rate variability information, wherein said heart rate variability information is based on a selected number of output QRS events;

periodically redetermining said heart rate variability information using at least some subsequently output QRS events;

during said period of time corresponding to the time period of the heart activity, displaying the most recently determined heart rate variability information.

2. A method of monitoring variability of heart activity occurring during a time period, comprising the steps of:

sequentially receiving data points of heart activity data over a period of time corresponding to the time period of the heart activity;

evaluating said data points as sequentially received to determine QRS events;

outputting said QRS events to a processor as they are sequentially determined;

processing said output QRS events as they are output to repeatedly determine a Chaotic Index of a selected group of determined QRS events, wherein said selected group of determined QRS events comprises X QRS events with said Chaotic Index being determined for sequential groups of X QRS events;

during said period of time corresponding to the time period of the heart activity, displaying the most recently determined Chaotic Index.

3. The method of claim 2, wherein X is 128.

4. A method of monitoring variability of heart activity occurring during a time period, comprising the steps of:

sequentially receiving data points of heart activity data over a period of time corresponding to the time period of the heart activity;

evaluating said data points as sequentially received to determine QRS events;

outputting said QRS events to a processor as they are sequentially determined;

processing said output QRS events as they are output to repeatedly determine time domain parameters, wherein said time domain parameters are first determined after a selected portion of said time period and repeatedly updated thereafter additionally using subsequent second selected groups of QRS events;

during said period of time corresponding to the time period of the heart activity, displaying the most recently determined time domain parameters.

5. The method of claim 4, wherein the determined time domain parameters are SDNN and RMSSD.

6. A method of monitoring variability of heart activity occurring during a time period, comprising the steps of:

sequentially receiving data points of heart activity data over a period of time corresponding to the time period of the heart activity;

evaluating said data points as sequentially received to determine QRS events;

outputting said QRS events to a processor as they are sequentially determined;

processing a selected number of output QRS events to determine a heart rate time series having a uniform interval for said selected number of most recently output QRS events, wherein said determined heart rate time series is updated after an additional Y number of QRS events are output using the most recently output selected number of QRS events;

processing said determined heart rate time series to determine a time-frequency distribution for the most recently updated heart rate time series;

displaying the most recently determined time-frequency distribution.

7. The method of claim 6, wherein said selected number is 256.

8. The method of claim 7, wherein Y is 40.

9. The method of claim 6, wherein said displaying step display uses intensity-mapped colors.

10. A method of monitoring variability of heart activity occurring during a time period, comprising the steps of:

sequentially receiving data points of heart activity data over a period of time corresponding to the time period of the heart activity;

evaluating said data points as sequentially received to determine QRS events;

outputting said QRS events to a processor as they are sequentially determined;

processing a selected number of output QRS events to determine a heart rate time series having a uniform interval for said selected number of most recently output QRS events, wherein said determined heart rate time series is updated after an additional Y number of QRS events are output using the most recently output selected number of QRS events;

processing said determined heart rate time series to determine a time-frequency distribution for the most recently updated heart rate time series;

processing the most recently determined time-frequency distribution to determine its spectral power in a low frequency range and its spectral power in a high frequency range of the t-f distribution;

displaying the most recently determined spectral power in the low frequency range and the spectral power in the high frequency range.

11. The method of claim 10, wherein said selected number is 256.

12. The method of claim 11, wherein Y is 40.

13. The method of claim 10, displaying the ratio of the most recently determined spectral power in the low frequency range to the most recently determined spectral power in the high frequency range.

14. The method of claim 10, wherein the low frequency range is 0.04 Hz to 0.15 Hz.

15. The method of claim 10, wherein the high frequency range is 0.15 Hz to 0.4 Hz.

16. A method of monitoring variability of heart activity occurring during a time period, comprising the steps of:

sequentially receiving data points of heart activity data over a period of time corresponding to the time period of the heart activity;

evaluating said data points as sequentially received to determine QRS events;

outputting said QRS events to a processor as they are sequentially determined;

processing said output QRS events as they are output to repeatedly determine a Chaotic Index of a selected group of determined QRS events, wherein said selected group of determined QRS events comprises X QRS events with said Chaotic Index being determined for sequential groups of X QRS events;

during said period of time corresponding to the time period of the heart activity, displaying the most recently determined Chaotic Index;

processing said output QRS events as they are output to repeatedly determine time domain parameters, wherein said time domain parameters are first determined after a selected portion of said time period and repeatedly updated thereafter additionally using subsequent second selected groups of QRS events;

during said period of time corresponding to the time period of the heart activity, displaying the most recently determined time domain parameters;

processing a selected number of output QRS events to determine a heart rate time series having a uniform interval for said selected number of most recently output QRS events, wherein said determined heart rate time series is updated after an additional Y number of QRS events are output using the most recently output selected number of QRS events;

processing said determined heart rate time series to determine a time-frequency distribution for the most recently updated heart rate time series;

displaying the most recently determined time-frequency distribution;

processing the most recently determined time-frequency distribution to determine its spectral power in a low frequency range and its spectral power in a high frequency range of the t-f distribution;

displaying the most recently determined spectral power in the low frequency range and the spectral power in the high frequency range.

17. The method of claim 16, wherein said selected number is 256.

18. The method of claim 17, wherein Y is 40.

19. The method of claim 16, wherein said data points of heart activity data are received during the heart activity.

20. The method of claim 16, wherein said data points of heart activity data are received from a pre-acquired file of data points of the heart activity.

21. A system for monitoring variability of heart activity occurring during a time period, comprising:

a heart activity data acquisition device adapted to acquire sequential data points of heart activity of a patient;

memory adapted to store sequential data points of heart activity in pre-acquired data files;

a user input for selecting between said acquisition device and a selected pre-acquired data file as a data source;

a processor adapted to

from said selected data source, sequentially receive data points of heart activity data over a period of time corresponding to the time period of the heart activity,

determine QRS events from said data points as sequentially received,

output said QRS events as they are sequentially determined,

repeatedly determine a Chaotic Index of a selected group of determined QRS events as they are output, wherein said selected group of determined QRS events comprises X QRS events

with said Chaotic Index being determined for sequential groups of X QRS events,

repeatedly determine time domain parameters from said QRS events as they are output, wherein said time domain parameters are first determined after a selected portion of said time period and repeatedly updated thereafter additionally using subsequent second selected groups of QRS events,

determine a heart rate time series having a uniform interval for a selected number of most recently output QRS events, wherein said determined heart rate time series is updated after an additional Y number of QRS events are output using the most recently output selected number of QRS events,

determine a time-frequency distribution for the most recently updated heart rate time series, and

for the most recently determined time-frequency distribution, determine spectral power in a low frequency range and its spectral power in a high frequency range;

a display continuously updated during said period of time corresponding to the time period of the heart activity to display the most recently determined Chaotic Index, the most recently determined time domain parameters, the most recently determined time-frequency distribution, the most recently determined spectral power in the low frequency range, and the most recently determined spectral power in the high frequency range.

22. The system of claim 21, wherein X is 128.

23. The system of claim 21, wherein said selected number is 256.

24. The system of claim 23, wherein Y is 40.

25. The system of claim 21, wherein processor includes function calls for Fast Fourier Transforms and Inverse Fast Fourier Transforms.

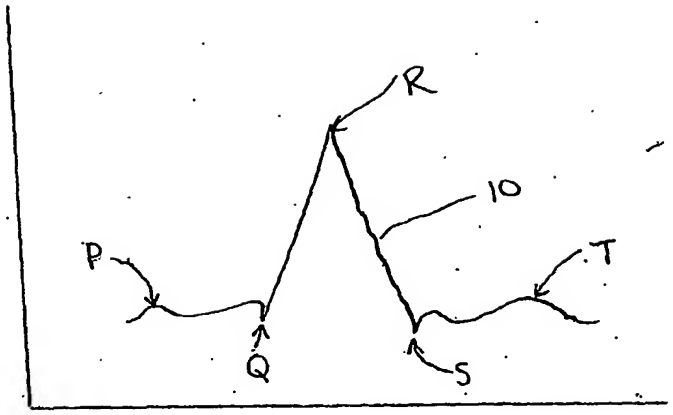


FIG. 1

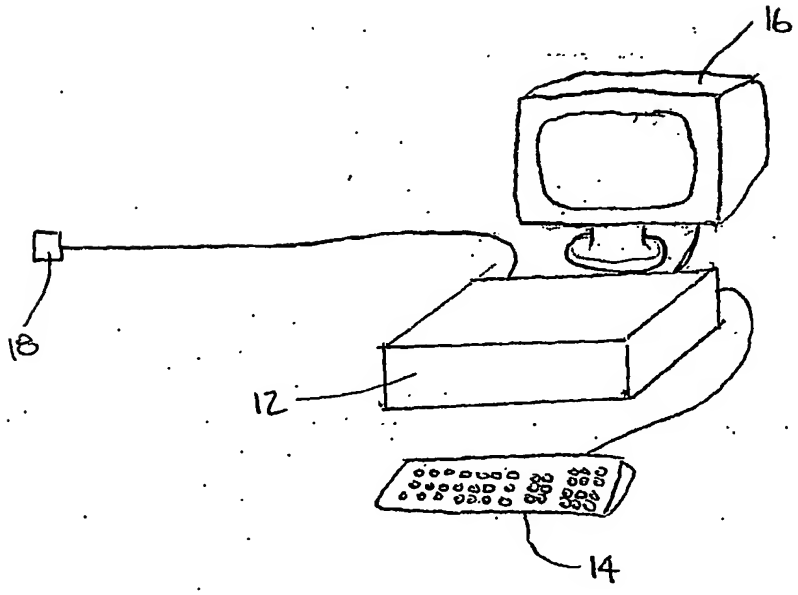
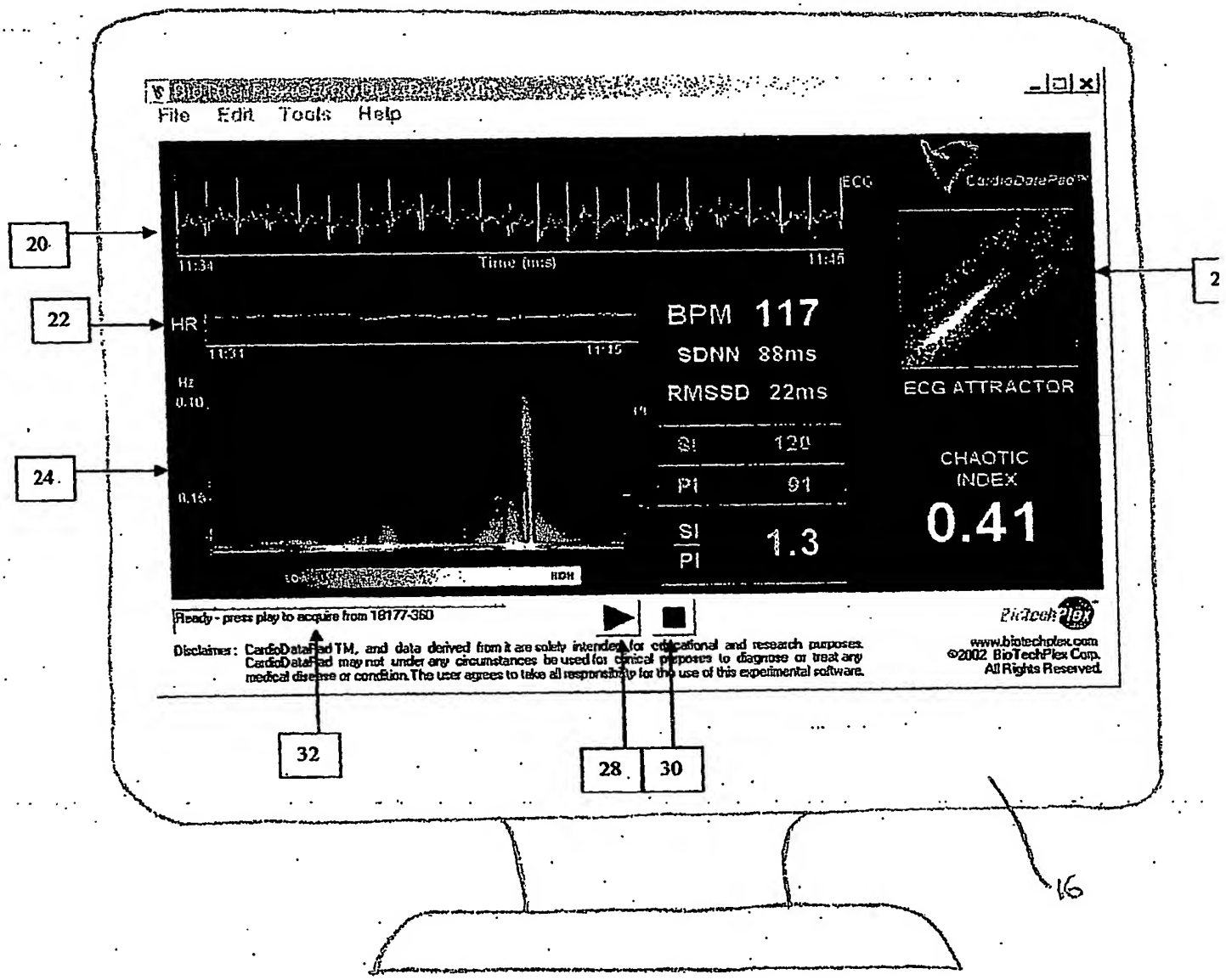


FIG. 2

Fig. 3


File Edit Tools Help
ECG
11:34
Time (m:s)
11:45
20
22
HR
11:31
11:15
Hz
0.10
0.15
24
BPM 117
SDNN 88ms
RMSSD 22ms
SI 120
PI 91
SI / PI 1.3
ECG ATTRACTOR
CHAOTIC INDEX
0.41
Ready - press play to acquire from 18177-360
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32
28
30
16

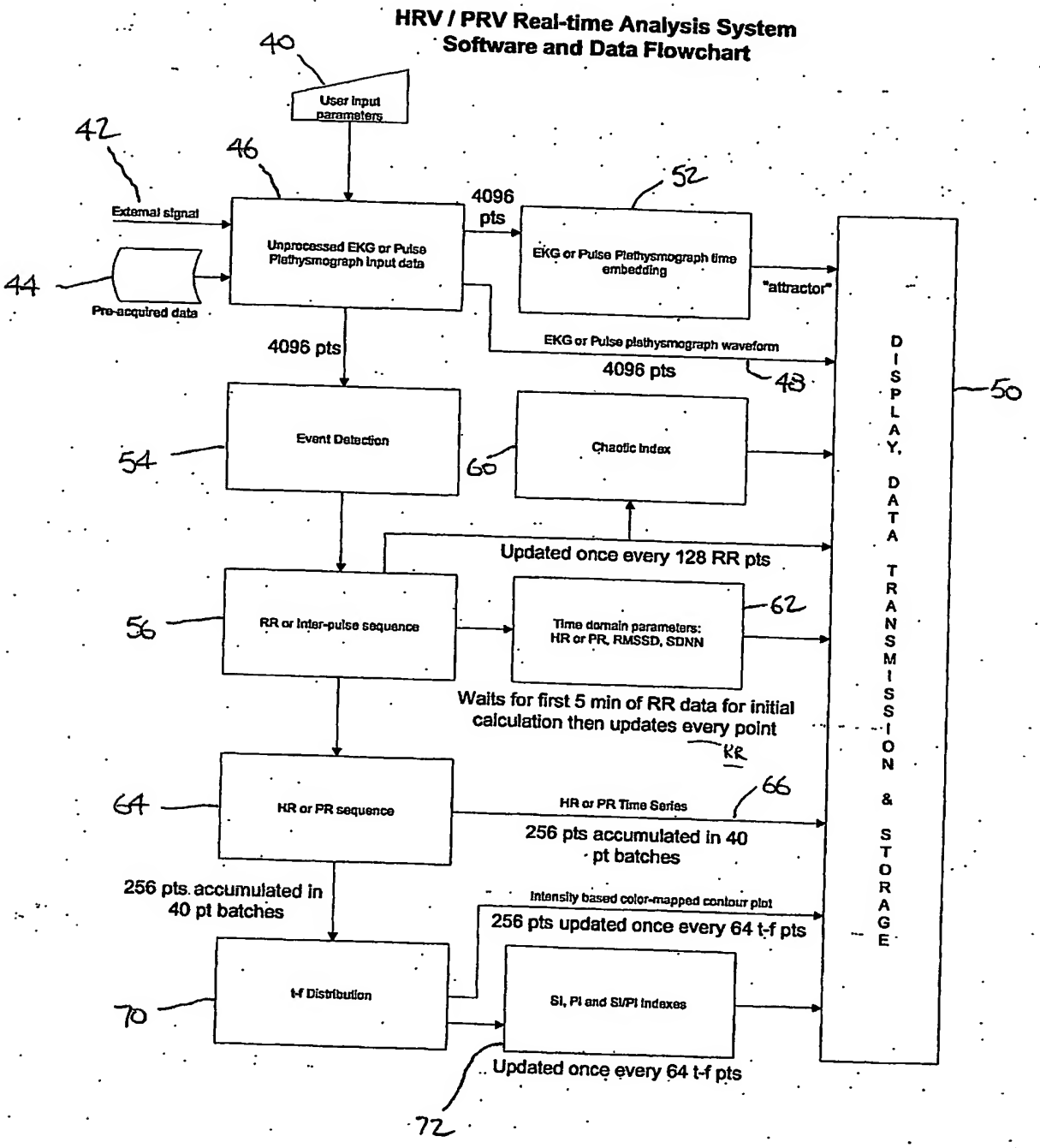
HRV / PRV Real-time Analysis System
Software and Data Flowchart
40
User input parameters
42
External signal
46
Unprocessed EKG or Pulse Plethysmograph input data
44
Pre-acquired data
4096 pts
52
EKG or Pulse Plethysmograph time embedding
"attractor"
4096 pts
EKG or Pulse plethysmograph waveform
4096 pts
48
50
DISPLAY, DATA TRANSMISSION & STORAGE
54
Event Detection
60
Chaotic Index
Updated once every 128 RR pts
56
RR or Inter-pulse sequence
Time domain parameters: HR or PR, RMSSD, SDNN
62
Waits for first 5 min of RR data for initial calculation then updates every point
RR
64
HR or PR sequence
HR or PR Time Series
66
256 pts accumulated in 40 pt batches
256 pts accumulated in 40 pt batches
Intensity based color-mapped contour plot
256 pts updated once every 64 t-f pts
70
t-f Distribution
SI, PI and SI/PI Indexes
Updated once every 64 t-f pts
72

FIG. 4

USER INPUT AND ECG ACQUISITION

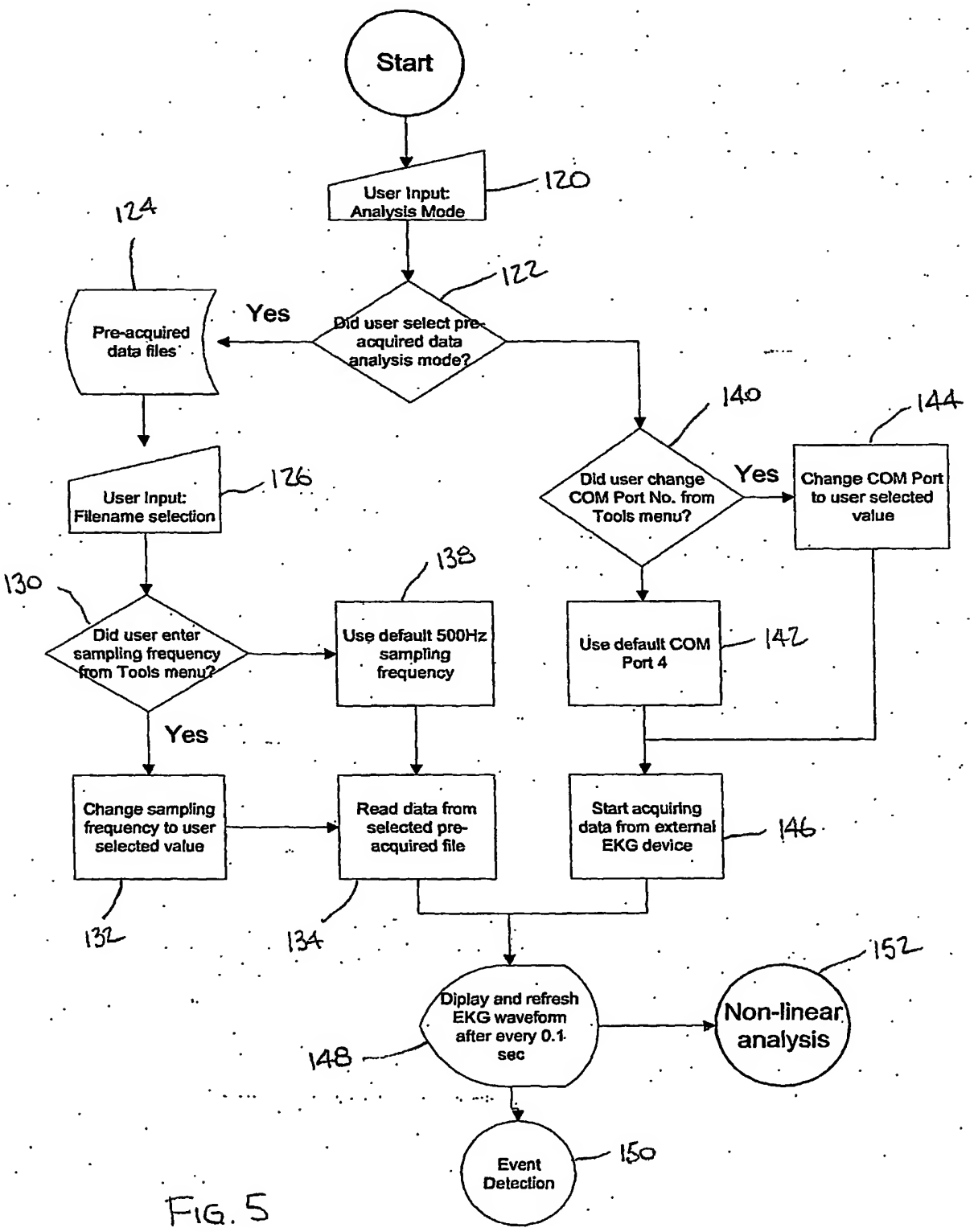

FIG. 5

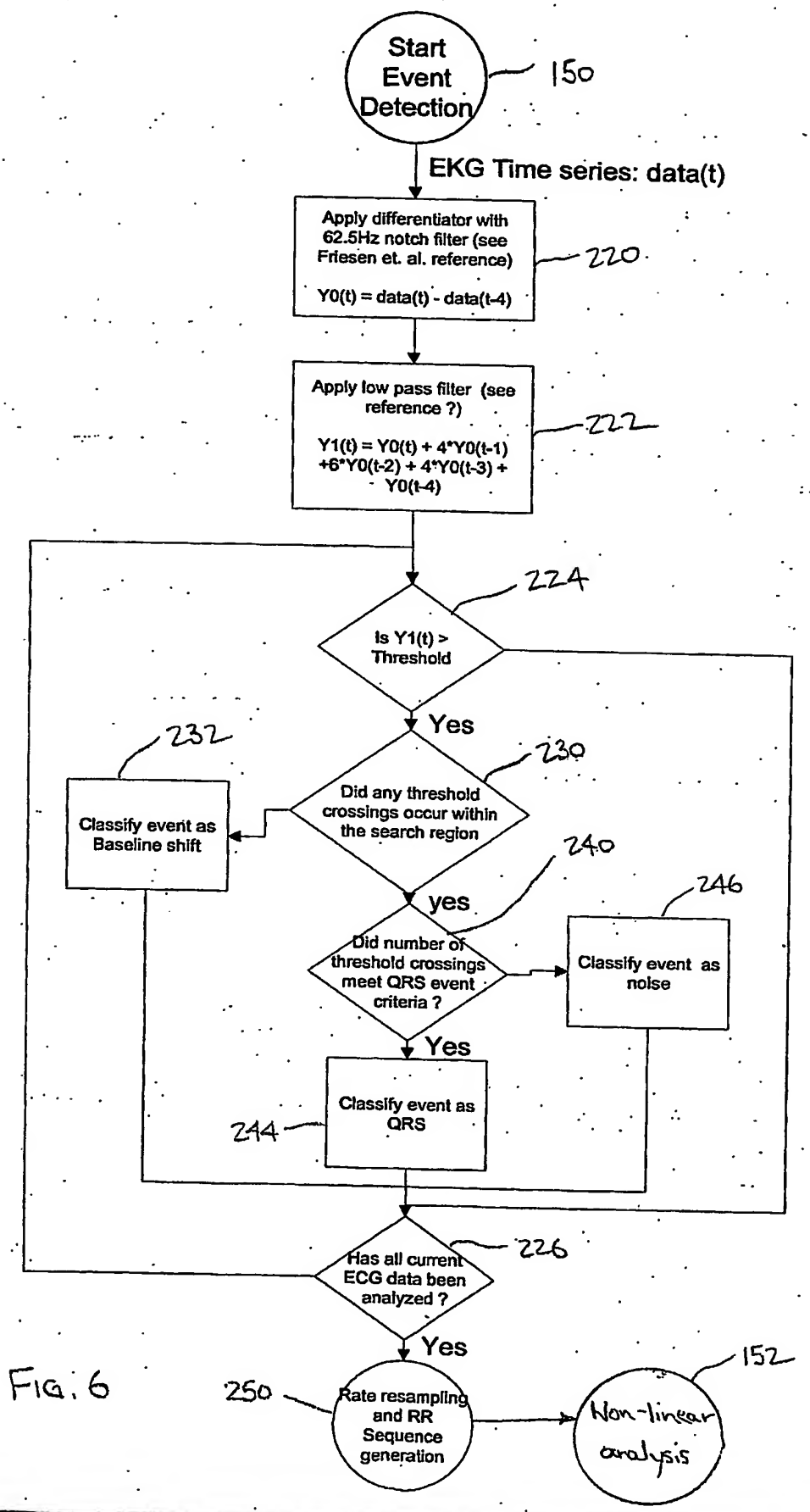
Start Event Detection
150
EKG Time series: data(t)
Apply differentiator with 62.5Hz notch filter (see Friesen et. al. reference)
Y0(t) = data(t) - data(t-4)
220
Apply low pass filter (see reference ?)
Y1(t) = Y0(t) + 4*Y0(t-1) +6*Y0(t-2) + 4*Y0(t-3) + Y0(t-4)
222
224
Is Y1(t) > Threshold
Yes
232
230
Did any threshold crossings occur within the search region
Classify event as Baseline shift
240
yes
246
Did number of threshold crossings meet QRS event criteria ?
Classify event as noise
Yes
Classify event as QRS
244
226
Has all current ECG data been analyzed ?
Yes
250
Rate resampling and RR Sequence generation
Non-linear analysis
152

Fig. 6

HEART RATE RESAMPLING AND SEQUENCE GENERATION ALGORITHM

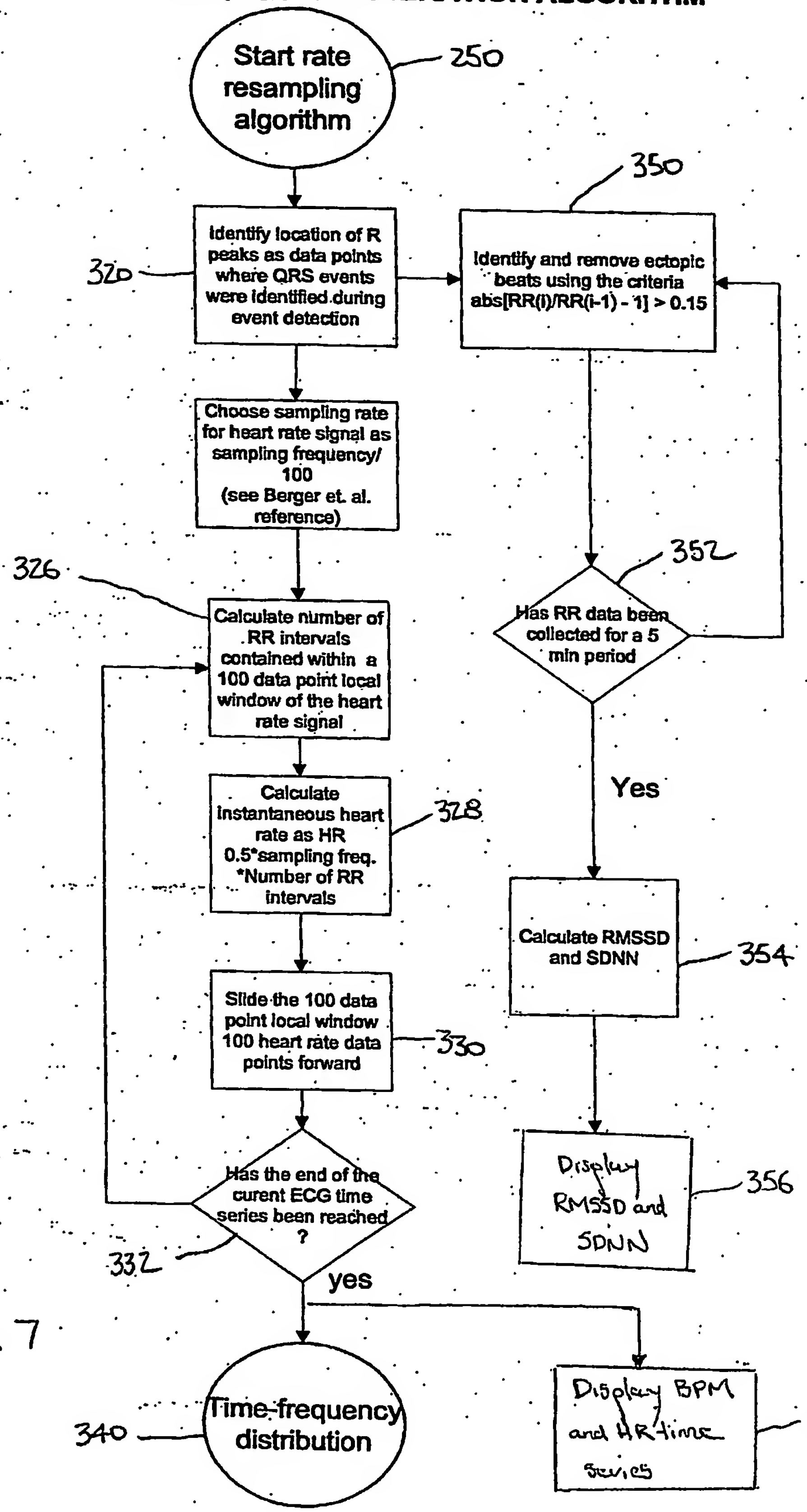

FIG. 7

TIME-FREQUENCY DISTRIBUTION

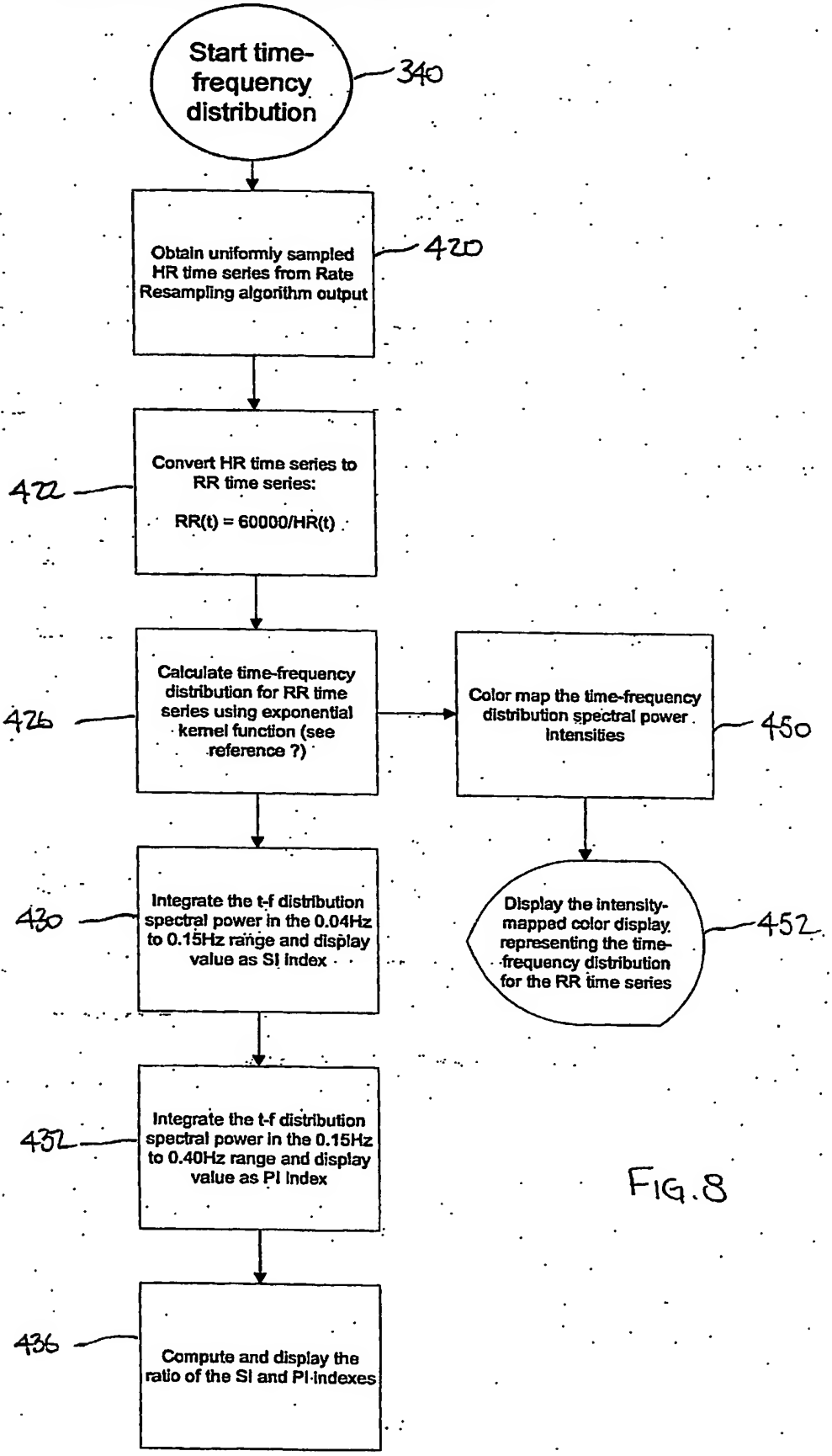

FIG. 8

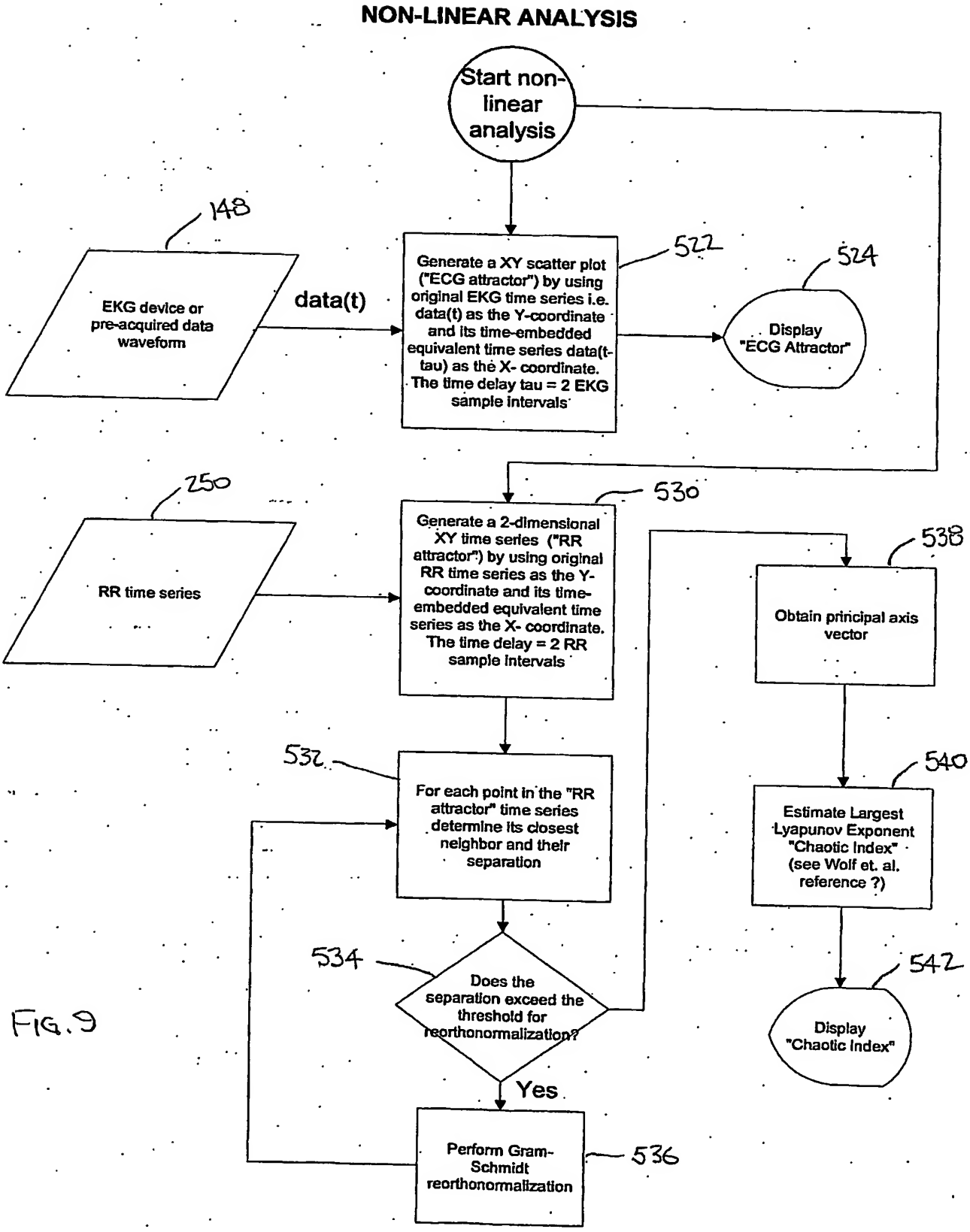
NON-LINEAR ANALYSIS
Start non-linear analysis
148
EKG device or pre-acquired data waveform
data(t)
Generate a XY scatter plot ("ECG attractor") by using original EKG time series i.e. data(t) as the Y-coordinate and its time-embedded equivalent time series data(t-tau) as the X- coordinate. The time delay tau = 2 EKG sample intervals
522
524
Display "ECG Attractor"
250
RR time series
Generate a 2-dimensional XY time series ("RR attractor") by using original RR time series as the Y-coordinate and its time-embedded equivalent time series as the X- coordinate. The time delay = 2 RR sample intervals
530
538
Obtain principal axis vector
532
For each point in the "RR attractor" time series determine its closest neighbor and their separation
540
Estimate Largest Lyapunov Exponent "Chaotic Index" (see Wolf et. al. reference ?)
534
Does the separation exceed the threshold for reorthonormalization?
542
Display "Chaotic Index"
Yes
Perform Gram-Schmidt reorthonormalization
536

FIG. 9

Figure 10A

```
EventStream::DetectEvents() // df1 version
{
    int *y0;
    int *y1;
    bool eventoccurred=false;

    y0=(int *)malloc(MAXDATASIZE*sizeof(int));
    y1=(int *)malloc(MAXDATASIZE*sizeof(int));


    for (int i=4; i<MAXDATASIZE;i++) {
        y0[i]=data[i]-data[i-4];
    }


    for (i=8;i<MAXDATASIZE;i++) {
        y1[i]=y0[i]+4*y0[i-1]+6*y0[i-2]+4*y0[i-3]+y0[i-4];
    }

    y1[0]=data[0]-prevdata[4]+4*(prevdata[7]-prevdata[3])+
        6*(prevdata[6]-prevdata[2])+4*(prevdata[5]-prevdata[1])+
        prevdata[4]-prevdata[0];
    y1[1]=data[1]-prevdata[5]+4*(data[0]-prevdata[4])+
        6*(prevdata[7]-prevdata[3])+4*(prevdata[6]-prevdata[2])+
        prevdata[5]-prevdata[1];
    y1[2]=data[2]-prevdata[6]+4*(data[1]-prevdata[5])+
        6*(data[0]-prevdata[4])+4*(prevdata[7]-prevdata[3])+
        prevdata[6]-prevdata[2];
    y1[3]=data[3]-prevdata[7]+4*(data[2]-prevdata[6])+
        6*(data[1]-prevdata[5])+4*(data[0]-prevdata[4])+
        prevdata[7]-prevdata[3];
    y1[4]=data[4]-data[0]+4*(data[3]-prevdata[7])+
        6*(data[2]-prevdata[6])+4*(data[1]-prevdata[5])+
        data[0]-prevdata[4];
    y1[5]=data[5]-data[1]+4*(data[4]-data[0])+
        6*(data[3]-prevdata[7])+4*(data[2]-prevdata[6])+
        data[1]-prevdata[5];
    y1[6]=data[6]-data[2]+4*(data[5]-data[1])+
        6*(data[4]-data[0])+4*(data[3]-prevdata[7])+
        data[2]-prevdata[6];
    y1[7]=data[7]-data[3]+4*(data[6]-data[2])+
        6*(data[5]-data[1])+4*(data[4]-prevdata[0])+
        data[3]-prevdata[7];

    if (detectcalls==0) {
        lastevent=0;
        prevlastevent=0;
        curevent=0;
    }
```

Figure 10B

```
eventcounter=0;
for (int j=0;j<MAXDATASIZE;j++)
    eventarray[j]=0;

for (i=0;i<58;i++) {
    if (prevy1[i]>200) {
        for (j=0;j<58;j++) {
            if (i+j>57) {
                if (y1[i+j-58]<-200)
                    eventoccurred=true;
                else
                    eventoccurred=false;
                if (eventoccurred)
                    break;
            }
            else
                if (prevy1[i+j]<-200)
                    eventoccurred=true;
                else
                    eventoccurred=false;
                if (eventoccurred)
                    break;
        } // end for j
    }
    else
        eventoccurred=false;
    if (eventoccurred) {
        if ((detectcalls*MAXDATASIZE+i-58-curevent)>100) {
            previastevent=lastevent;
            lastevent=curevent;
            curevent=detectcalls*MAXDATASIZE+i-58;
            if (curevent-lastevent>1000) {
                lastevent=curevent;
                previastevent=curevent;
            }
            else {
                rrarray[rrcounter]=curevent-lastevent;
                rrcounter++;
            }
        }
    }
} // end for i


for (i=0;i<MAXDATASIZE-58;i++) {

    if (y1[i]>200){
        for (j=0;j<58;j++) {
            if (y1[i+j]<-200) {
                eventoccurred=true;
            }
            else
                eventoccurred=false;
            if (eventoccurred)
                break;
        } // end for j
    }
    else
        eventoccurred=false;
```

Figure 10C

```
if (eventoccurred) {
        if ((detectcalls*MAXDATASIZE+i-curevent)>100) { // High HR reject

                prevlastevent=lastevent;
                lastevent=curevent;
                curevent=detectcalls*MAXDATASIZE+i;

                if (curevent-lastevent>1000) { // low HR reject
                        lastevent=curevent;
                        prevlastevent=lastevent;
                }
                else {
                        rrarray[rrcounter]=curevent-lastevent;
                        rrcounter++;
                }

                while (detectcalls*MAXDATASIZE+eventcounter<curevent-50
                        && prevlastevent<lastevent-100
                        && lastevent<curevent-100) { // exception for first run and skips

                        if (detectcalls*MAXDATASIZE+eventcounter<lastevent-50){
                                eventarray[eventcounter]=60.0f*samplerate/(lastevent-
prevlastevent);
                        }
                        else if (detectcalls*MAXDATASIZE+eventcounter<lastevent+50){
                                int portioninlast=lastevent-(detectcalls*MAXDATASIZE+
                                        eventcounter);
                                float numberofrrintervals=
                                        (50.0f+(float)portioninlast)/
                                        ((float)lastevent-(float)prevlastevent)+
                                        (50.0f-(float)portioninlast)/
                                        ((float)curevent-(float)lastevent);
                                eventarray[eventcounter]=numberofrrintervals/
                                        (100.0f/(float)samplerate)*60.0f;
                        }
                        else if (detectcalls*MAXDATASIZE+eventcounter<curevent-50) {
                                eventarray[eventcounter]=60.0f*samplerate/(curevent-
lastevent);
                        }
                        eventcounter+=100;
                } // end while
        } // end if
    } // end if
} // end for

for (i=0;i<8;i++)
    prevdata[i]=data[MAXDATASIZE-8+i];

for (i=0;i<58;i++)
    prevy1[i]=y1[MAXDATASIZE-58+i];

detectcalls++;
free(y0);
free(y1);
return(0);
```

Fig. 11

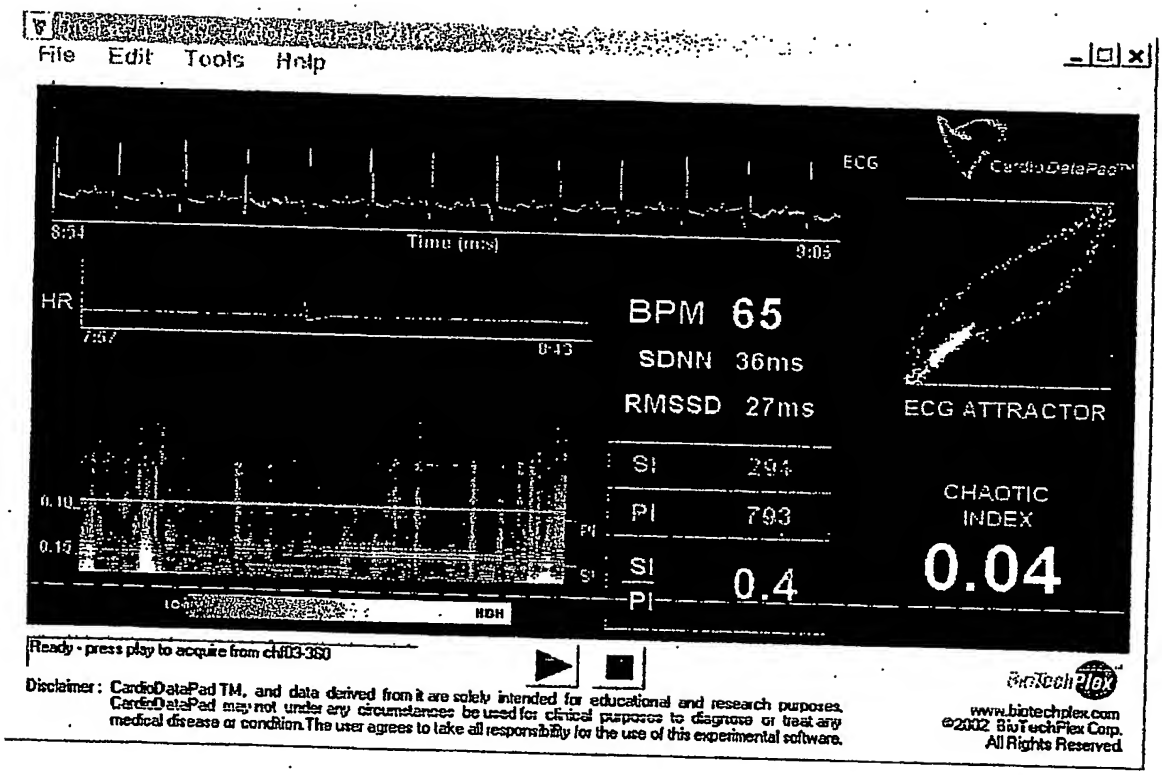
File Edit Tools Help
ECG
8:54
Time (ms)
9:05
HR
7:57
8:13
BPM 65
SDNN 36ms
RMSSD 27ms
SI 294
PI 793
SI/PI 0.4
ECG ATTRACTOR
CHAOTIC INDEX
0.04
0.10
0.10
PI
SI
HDH
Ready - press play to acquire from chf03-350
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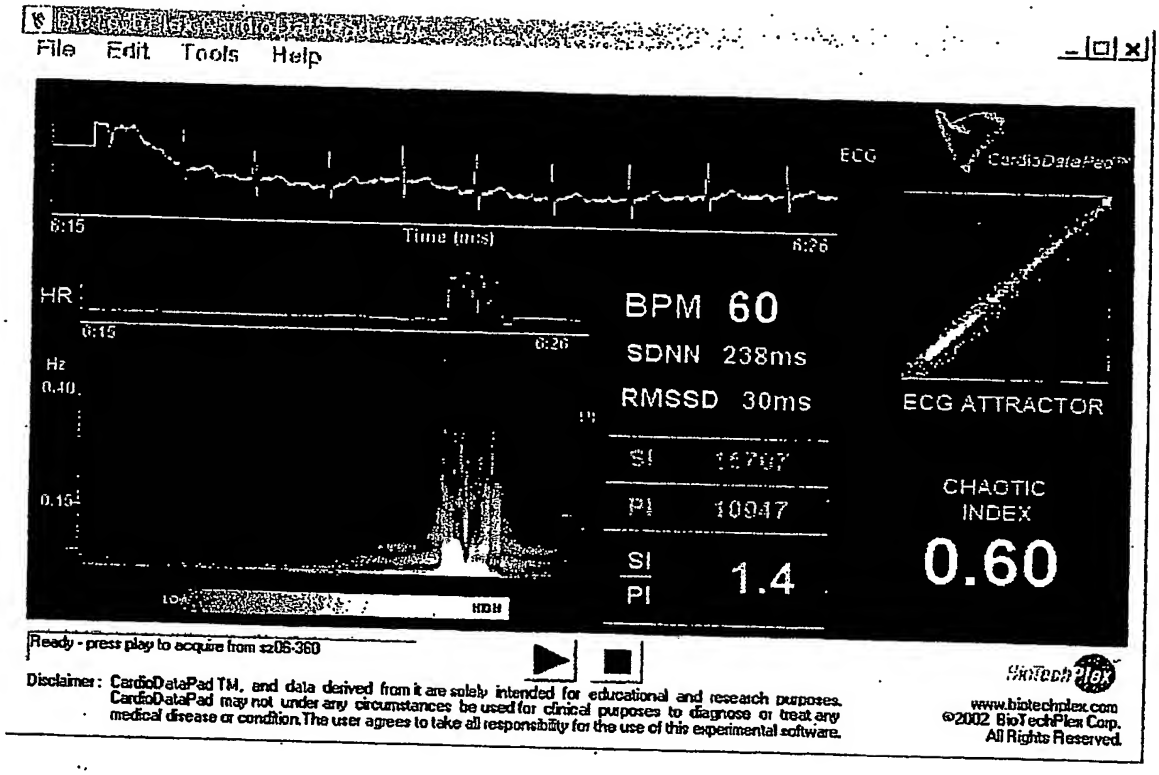
Fig. 12


File Edit Tools Help
ECG
6:15
Time (ms)
6:26
HR
6:15
6:26
Hz
0.40
0.15
LOW
HIGH
BPM 60
SDNN 238ms
RMSSD 30ms
SI 15707
PI 10947
SI
PI 1.4
CardioDataPad™
ECG ATTRACTOR
CHAOTIC INDEX
0.60
Ready - press play to acquire from sz06-360
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